

The opinion in support of the decision being entered today is not binding precedent of the Board.

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

RANDOLPH NOELLE

Junior Party,
(Application 08/742,480),

v.

RICHARD J. ARMITAGE,
WILLIAM C. FANSLOW, and MELANIE K. SPRIGGS

Senior Party,
(Application 09/322,021).

Patent Interference No. 104,724

Before: TORCZON, GARDNER-LANE, and NAGUMO, Administrative Patent Judges.

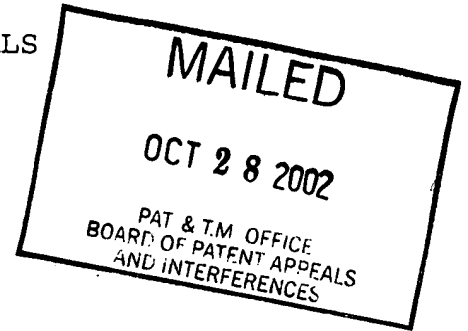
NAGUMO, Administrative Patent Judge.

JUDGMENT

(PURSUANT TO 37 C.F.R. § 1.640)

INTRODUCTION

This proceeding relates to monoclonal antibodies ("mAb") that bind to the antigen CD40CR, which is expressed on activated T cells. The binding of the mAb interferes with the activation of B cells by activated T cells.



Junior party Noelle has filed one miscellaneous motion; senior party Armitage has file three preliminary motions. Oral argument was held on 24 July 2002. Mr. E. Anthony Figg, Esq., accompanied by Mr. Erik van Leeuwen, argued for Noelle; Mr. Gordon Kit, Esq., argued for Armitage.

BACKGROUND

The following findings of fact are supported by a preponderance of evidence in the record.

The parties

Noelle

1. Noelle's involved 08/742,480 ('480) application was filed 1 November, 1996. Noelle has been accorded the benefit for priority in this proceeding of the following applications:

application	filing date
08/338,975	14 November 1994
07/835,799	14 February 1992

The application is entitled "CD40CR receptor and ligands thereof."

2. Randolph Noelle is the sole named inventor for the '480 application.

3. The Trustees of Dartmouth College is Noelle's real party in interest.

4. Noelle's claims 42, 43, 46-48, 50, 54 and 57 correspond to the count.

5. Noelle's claims 45, 51-53, 55, 56, 59, and 60 do not correspond to the count and are not a part of this interference.

Armitage

6. Armitage's involved 09/322,021 ('021) application was filed 28 May 1999. Armitage has been accorded the benefit for priority in this proceeding of the following applications:

Application	filing date
08/249,189	24 May 1994
07/969,703	23 October 1992
07/805,723	5 December 1991
07/783,707	25 October 1991

7. The named inventors of the '021 application are Richard J. Armitage, William C. Fanslow, and Melanie K. Spriggs.

8. Immunex Corporation, which is a wholly-owned subsidiary of Amgen, is Armitage's real party in interest.

9. All of Armitage's claims, 28, 29, and 30, correspond to the count.

The count

10. The count is claim 42 of Noelle or claim 28 or claim 29 or claim 30 of Armitage. In summary, it is a monoclonal antibody or a fragment thereof, or a pharmaceutical composition comprising the monoclonal antibody, or a hybridoma that produces the monoclonal antibody.

11. Noelle's claim 42 reads as follows:

A monoclonal antibody or fragment thereof which specifically binds to an antigen expressed on activated T cells, wherein said antigen is specifically bound by the monoclonal antibody secreted by hybridoma MR1 which hybridoma has been deposited an accorded ATCC Accession No. HB 11048.

12. Armitage's claim 28 reads as follows:

A monoclonal antibody that binds to mouse CD40L encoded by vector pDC406-mCD40-L having ATCC Accession No. 68872.

13. Armitage's claim 29 reads as follows:

A pharmaceutical composition comprising a monoclonal antibody according to claim 28, and a pharmaceutially acceptable carrier.

14. Armitage's claim 30 reads as follows:

A hybridoma which secretes a monoclonal antibody that binds to mouse CD40L encoded by vector pDC406-mCD40-L having ATCC accession No. 68872.

Technical Background

15. An antigen is a foreign substance, usually a protein, that triggers an immune (antibody) reaction in a host animal.

16. An antibody is a protein that specifically recognizes and binds to a specific antigen. The site on the antigen recognized by an antibody is called an "epitope."

17. Antibodies generally are shaped like a capital Y. There are two types of fragments that recognize antigens:

$F(ab')_2$ is a bivalent fragment that can bind to two (identical) epitopes. It corresponds to the upper arms of the Y;

Fab is a monovalent fragment that can bind to a single epitope. It corresponds to one of the upper arms of the Y.

A third fragment, Fc, corresponds to the stem of the Y, and does not bind to antigens. (AX1008.)

18. Antibodies consist of four polypeptide chains, two identical light chains, and two identical heavy chains. Each light chain contains one variable and one constant domain. Each heavy chain contains one variable and three constant domains. Each arm of the antibody is formed from one light chain that is linked to the variable and a constant region of the heavy chain by a disulfide (-S-S-) linkage. The site that binds to the epitope on the antigen is in the variable region of the antibody. The stem of the antibody is formed from the remaining constant regions of the heavy chains, which are linked by a pair of disulfide linkages. (AX1008.)

19. Antibodies recognize antigens by binding to specific regions of the antigens called "epitopes." An epitope is like a key that will exactly fit the lock of a particular antibody. Such binding is called "specific binding," in contrast to nonspecific binding, in which antibodies bind indiscriminately to molecules other than the specific antigen at non-lock-and-key positions.

20. B cells are lymphocytes (white blood cells) that make and secrete antibodies. Each cell is programmed to make a specific antibody that recognizes a single specific antigen.

21. B cells carry a protein called "CD40" on the surface of the cell.

22. Helper T cells, T_h , are lymphocytes that originate in the thymus gland.

23. Activated T_h cells carry a protein called CD40CR that binds specifically to the CD40 protein carried on the surface of B cells. In the record, CD40CR is also denoted by terms including "CD40L," and "CD40 ligand." The term CD40CR will be used throughout this decision.

24. The binding of CD40CR to CD40 stimulates the B cells to make antibodies.

25. Antibody formation can be harmful when the body makes too many antibodies, as in allergies, anaphylactic shock, and autoimmune diseases such as lupus. (AX1001 at 4.)

26. Noelle discovered an antibody to CD40CR that binds to the CD40CR on activated T cells. The binding blocks the interaction of the activated T cells with B cells. As a result, the B cells are not activated to make antibodies.

27. Monoclonal antibodies (mAb) are made by cells that are fusions between antibody-producing cells and immortal (tumor-like) B cells. If the fused cells, which are called hybridomas,

are isolated and selected for production of a particular antibody, they can be grown in large quantities and the antibodies produced will be identical, all recognizing a single antigen.

28. MR1 is a hybridoma developed by Noelle that secretes large amounts of a single (monoclonal) antibody against CD40CR.

29. Noelle's specification states that "[t]he present invention, which relates to the antigen nonspecific CD40/CD40CR interaction, circumvents the need to characterize to antigen associated with allergy or autoimmunity. Therefore, the present invention may be used to particular advantage in the treatment of allergic conditions in which the immunogen is not known" (AX1001 at 3-4.) In other words, the action of the antibody to CD40CR is thought to be independent of the type of antibody produced by the B cell.

30. A chimeric antibody is "[a]n antibody that contains proteins from different species (e.g., murine/human monoclonal antibodies." (AX1017.)

31. Noelle's claim 46, which corresponds to the count, reads as follows:

46. The monoclonal antibody or fragment of Claim 42, which is selected from the group consisting of a chimeric antibody, a human monoclonal antibody, a F(ab')₂ fragment, and a Fab fragment.

32. Noelle's specification states that "[t]he present invention also provides for chimeric antibodies produced by

techniques known in the art, such as those set forth in Morrison et al. [AX 1018] or [AX1019]." (AX1001 at 12.)

33. Morrison teaches making chimeric antibodies using recombinant DNA techniques in which the variable region genes of a mouse antibody-producing myeloma cell lines are joined to human immunoglobulin constant region genes. (AX1018 at 6851; AX1019 abstract, and at 2.) Thus, in order to use Morrison's teachings to make chimeric antibodies, one needs the DNA sequence of at least the relevant part of each antibody that is to contribute to the chimeric antibody.

34. Noelle's specification provides no other teaching of techniques that are well known in the art to make chimeric antibodies, monoclonal or otherwise.

35. Noelle has not cited in its briefing to the Board in this case any other teachings in the record regarding the production of chimeric monoclonal antibodies.

Noelle's motion

36. Noelle filed a miscellaneous motion to suppress certain evidence allegedly submitted by Armitage for the first time with Armitage's Reply Briefs.

Armitage's motions¹

37. Armitage filed the following preliminary motions:

a. Preliminary motion 1 that various of Noelle's claims are unpatentable under 35 U.S.C. § 112, first paragraph, for lack of adequate written description and lack of an enabling disclosure; that Noelle's claims are unpatentable under 35 U.S.C. § 112, second paragraph, because they do not claim the invention of interest to Noelle; and that Noelle's dependent claims are unpatentable under 35 U.S.C. § 112, fourth paragraph because they fail to further limit the claims from which they depend.

b. Preliminary motion 2 that Noelle's claims are unpatentable under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103 over Armitage et al., WO 93/08207. (This motion is effectively contingent on the granting of Armitage's preliminary motion 1.)

c. Preliminary motion 3 that Noelle's claims are unpatentable under 35 U.S.C. § 102(e) or under 35 U.S.C. § 103 over U.S. Patent 5,961,974, issued to Armitage et al., which has an effective filing date of October 25, 1991.

Armitage's Preliminary Motion No. 1

38. Armitage's Preliminary Motion No. 1 raises some seven challenges to the legitimacy of Noelle's claims under the first paragraph of § 112. Generally, Armitage argues that Noelle's

¹ Armitage's preliminary motions are cited as "APM1 at __," etc. Noelle's oppositions are cited as "NOPP1 at __," etc. Armitage's replies are cited as "AR1 at __," etc.

specification does not provide an adequate written description of the claimed invention to show that Noelle was in possession of the entire scope of the claimed subject matter. Moreover, according to Armitage, Noelle's disclosure does not provide an enabling description, such that one of ordinary skill in the art would require undue experimentation to make and use the full scope of the claimed invention. For reasons given *post*, we need describe and consider in detail only Armitage's second argument for lack of enablement.

39. Armitage's second argument is that all the claims are generic to chimeric monoclonal antibodies, but that the only way disclosed to make such antibodies requires the DNA corresponding to the antibody, which was admittedly unknown when Noelle filed its application.

40. Armitage's preliminary motion no. 1 further urges that certain of Noelle's claims are unpatentable under 35 U.S.C. § 112, second paragraph, and that certain of Noelle's claims are unpatentable under 35 U.S.C. § 112, fourth paragraph.

Armitage's Preliminary Motion No. 2

41. Armitage's Preliminary Motion No. 2 is premised on the failure of Noelle's application to provide an enabling disclosure of chimeric monoclonal antibodies until 14 November 1994, or until 1 November 1996, i.e., after Armitage had disclosed the DNA sequence corresponding to CD40CR. Accordingly, Armitage argues

that Noelle's involved claims 42, 43, 46-48, 50, 54, and 57 are unpatentable under 35 U.S.C. § 102(b) or under 35 U.S.C. § 103 over Armitage et al. WO 93/08207 (AX1022).

Armitage's Preliminary Motion No. 3

42. Armitage's preliminary motion no. 3 urges that Noelle's involved claims 42, 43, 46-48, 50, 54, and 57 are unpatentable under 35 U.S.C. §§ 102 and 103 over U.S. Patent No. 5,961,974, issued to Armitage et al. (AX1020). Armitage's arguments are founded on its assertion that Noelle's preliminary statement is insufficient. Noelle responds that it has followed procedures approved by the Trial Section of the Board, and that the issue should be deferred to final hearing.

DISCUSSION

Patentability of Noelle's Claims under 35 U.S.C. § 112, first paragraph

Armitage challenges the scope of Noelle's claims as not reasonably commensurate with the enabled scope of Noelle's disclosure. "As a result," Armitage argues, the challenged claims "lack written description and are indefinite and not enabled. Hence, they are unpatentable under 35 U.S.C. § 112, first paragraph." (APM1 at 14, 16, and 18-21.)

The law of written description, particularly when a biological deposit has been made in support of the claimed subject matter under 37 C.F.R. § 1.801 et seq., underwent a

tumultuous period during and subsequent to the briefing period for these motions. The Court of Appeals for the Federal Circuit issued its initial decision in *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 285 F.3d 1013, 62 USPQ2d 1289 (Fed. Cir. 2002) ("*Enzo I*") on April 2, 2002, after Noelle and Armitage had filed their preliminary motions but before they had filed their oppositions. The Federal Circuit subsequently vacated its *Enzo I* decision in *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002) ("*Enzo II*") on July 15, 2002, after the completion of briefing. As a result, the parties could not brief the issue of the adequacy of the written description in the case before us in light of the Federal Circuit's holding that, in some cases, a "reference in the specification to a deposit in a public depository, which makes its contents accessible to the public when it is not otherwise available in written form, constitutes an adequate description of the deposited material sufficient to comply with the written description requirement of § 112, ¶ 1." *Enzo II*, 296 F.3d at 1325, 63 USPQ2d at 1613. In the absence of elucidation and analysis by the parties of relevant facts in the record, we decline to base our decision in this case on the written description requirement. At oral hearing, the parties concentrated on the enablement aspects of Armitage's Preliminary Motion No. 1. (See the Transcript and corrections, Papers 58-60.)

Chimeric mAb

We need consider only Armitage's challenge to the enablement of the disclosure relating to chimeric monoclonal antibodies, as we find this issue dispositive. Noelle's claim 42 reads as follows:

42. A monoclonal antibody or fragment thereof which specifically binds to an antigen expressed on activated T cells, wherein said antigen is specifically bound by the monoclonal antibody secreted by hybridoma MR1 which hybridoma has been deposited an accorded ATCC Accession No. HB 11048.

Noelle's claim 46 reads as follows:

46. The monoclonal antibody or fragment of Claim 42, which is selected from the group consisting of a chimeric antibody, a human monoclonal antibody, a F(ab')₂ fragment, and a Fab fragment.

Thus claim 42 (and each of the other dependent claims, none of which excludes chimeric antibodies) encompasses chimeric antibodies.

Armitage argues that Noelle did not disclose the DNA sequence (e.g., the gene) corresponding to any mAb that binds to CD40CR. Armitage argues further that the only method taught by Noelle as being useful for making chimeric monoclonal antibodies - that of Morrison (AX1018, AX1019) - requires knowledge of such a DNA sequence. Armitage concludes that, absent such a sequence, Noelle did not provide an enabling disclosure of chimeric antibodies.

Noelle concedes that it did not know the genetic code (DNA) corresponding to the MR1 antibody as of 14 February 1992. (NOPP1 at 3, admitting Armitage's fact 5 (APM1 at 4).) Noelle contends, however, that "[s]uch chimeric antibodies were obtainable using standard biochemical methods known to persons of ordinary skill in 1992 without having to first obtain the DNA molecule of any antibody component." (NOPP1 at 18.) At oral argument, Noelle also argued that it was routine to obtain the necessary DNA, and that such experimentation would therefore not be "undue":

"Morrison tells you once you have that hybridoma, you clone the DNA and you engineer the DNA to make hybrid antibodies, chimeric antibodies. There is absolutely no evidence on the Armitage side that would involve undue experimentation, that a person skilled in the art would think that that involved any undue experimentation or was anything beyond routine."

(Proceeding Transcript at 37, ll. 13-20.) Noelle concludes that it has met the enablement requirement.

Whether one of ordinary skill in this art would have been required undue experimentation to make chimeric monoclonal antibodies requires consideration of the "*Wands*" factors. These factors include: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404

(Fed. Cir. 1988), *citing with approval Ex parte Forman*, 230 USPQ 526, 547 (Bd. Pat. App. & Int. 1986). We remain mindful that the *Wands* list is neither complete nor mandatory. *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1371, 52 USPQ2d 1129, 1136 (Fed. Cir. 1999) ("all of the [*Wands*] factors need not be reviewed when determining whether the disclosure is enabling."); *Amgen Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) ("[*Wands* factors] are illustrative, not mandatory. What is relevant depends on the facts.")

We find the quantity of experimentation necessary to obtain chimeric monoclonal antibodies to CD40CR, at the relevant time, to have been extensive, based on the disclosures in the two interfering specifications. The state of the prior art and the relative skill of those in the art are highly sophisticated, as shown by the specifications, prior art of record, and the deposition testimony of record. Certain aspects of the antibody art are generally accepted as routine. See, e.g., *Hybritech Inc. v. Monoclonal Antibodies*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986) (holding that screening for necessary characteristics were routine). However, the nature of the present invention is a highly technical and indeed somewhat speculative attempt to modify the extremely complex and as yet incompletely understood interactions between T cells and B cells. As already noted, there is minimal guidance and no working

example in Noelle's specification regarding chimeric mAbs. Moreover, the "predictability" asserted by Noelle is little more than a statement that the genetic code corresponding to any identified antibody can, eventually, be determined. In particular, there are insufficient data to have permitted a reasonably confident prediction of whether a particular chimeric mAb prepared by any technique would work for its intended purpose of blocking B cell activation by activated T cells at the time of Noelle's first filing. Finally, the scope of Noelle's claims are extremely broad. They encompass all chimeric monoclonal antibodies from any combination of species, the sole limitation being that they recognize the same antigen recognized by the MR1 antibody.

The only factor weighing in favor of Noelle vis-à-vis enablement via recombinant DNA techniques is the high level of skill in the art. The minimal guidance provided in this pioneering invention in an uncertain art does not direct one of skill towards any particular DNA. At best, it invites one to go find the DNA that everyone knew would exist, once the antibody was demonstrated. On this record, Noelle has not provided enough of a foundation for the CD40CR protein to enable others to make and use, without undue experimentation, chimeric mAb via recombinant DNA techniques.

Noelle's position that "standard biochemical techniques" for making chimeric antibodies that do not involve using recombinant DNA methods is unsupported by citation to the prior art of record. It is true that an applicant need not teach in its specification what is well known in the art. *Hybritech*, 802 F.2d at 1384, 231 USPQ at 94 ("a patent need not teach, and preferably omits, what is well known in the art"). However, when, as here, a *prima facie* case of unpatentability has been established based on the sole method mentioned in its specification, a party may not rely on mere argument that other, unmentioned methods were well known at the time of the invention. Mere arguments cannot take the place of evidence in the record. *Estee Lauder, Inc. v. L'Oreal, S.A.*, 129 F.3d 588, 595, 44 USPQ2d 1610, 1615 (Fed. Cir. 1997). Moreover, we shall not take it upon ourselves to mine the record for evidence in support of one party or the other. *In re Swartz*, 232 F.3d 862, 864, 56 USPQ2d 1703, 1704 (Fed. Cir. 2000) (declining an invitation to peruse the record).

Given the failure to substantiate a disclosed method of obtaining chimeric monoclonal antibodies by "standard techniques," the preponderance of the evidence persuades us that the amount of experimentation required to make them by any technique would have been "undue." Thus, we cannot say that Noelle has established any basis on which it might be said that the scope of the claimed subject matter bears a reasonable

correspondence to the disclosed and enabled subject matter. As our reviewing court has stated recently, "when there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply to novel aspects of an invention in order to constitute adequate enablement."

Genentech, Inc. v. Novo Nordisk, A/S, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997). Accordingly, we hold that Noelle's specification does not provide an enabling disclosure of chimeric monoclonal antibodies that bind to the same antigen as does the antibody produced by MR1.

To this extent, Armitage's Preliminary Motion No. 1 is granted. As Armitage has correctly noted, all of Noelle's claims encompass chimeric monoclonal antibodies. Accordingly, all of Noelle's claims that correspond to the count in this interference, namely claims 42, 43, 46-48, 50, 54, and 57, are unpatentable for lack of an enabling disclosure.

The remaining issues raised by Armitage under 35 U.S.C. § 112, and the issues raised in Armitage's preliminary motions 2 and 3 are moot.

As we have not relied on any of the evidence that Noelle objects to in its miscellaneous motion No. 1, we need not consider that motion. We observe that Noelle has not filed any other motions, e.g., to redefine the count by amending a claim corresponding to the count (37 C.F.R. § 1.633(c)(2)).

ORDER

Upon consideration of the motions, it is:

ORDERED that Armitage's preliminary motion be GRANTED on the ground that Noelle's claims 42, 43, 46-48, 50, 54, and 57 are not enabled for chimeric monoclonal antibodies, but otherwise DISMISSED;

FURTHER ORDERED that Armitage's preliminary motions 2 and 3 be DISMISSED as moot;

FURTHER ORDERED that Noelle's miscellaneous motion 1 be DISMISSED as moot;


FURTHER ORDERED that Noelle is not entitled to a patent containing claims 42, 43, 46-48, 50, 54, and 57;

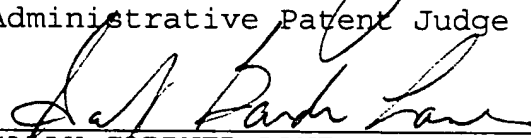
FURTHER ORDERED that any request for reconsideration of this decision be filed **within three weeks of the date this decision is mailed**;

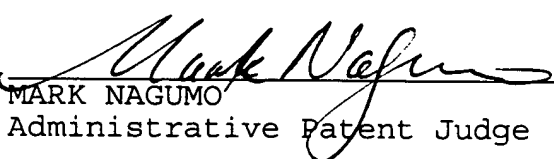
FURTHER ORDERED that this interference judge be remanded to Administrative Patent Judge Nagumo, who has been assigned to the interference;

FURTHER ORDERED that if there is a settlement agreement, attention is directed to 35 U.S.C. § 135(c) and 37 C.F.R. § 1.661; and

FURTHER ORDERED that a copy of this decision be given a paper number and be entered in the administrative records of Noelle' application 08/742,480 and of Armitage's application 09/322,021.



RICHARD TORCZON
Administrative Patent Judge)
)


SALLY GARDNER-LANE
Administrative Patent Judge)
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BOARD OF PATENT
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